NCBI Entrez **Protein QUERY** BLAST Entrez ?

Other Formats: FASTA | Graphic

Links: DNA | Related Sequences

LOCUS 1877288 200 aa 17-JUN-1998
DEFINITION hypothetical protein Rv3557c.
ACCESSION 1877288
PID g1877288
DBSOURCE EMBL: locus MTCY6G11, accession Z92774
KEYWORDS .
SOURCE Mycobacterium tuberculosis.
ORGANISM Mycobacterium tuberculosis
Bacteria; Firmicutes; Actinobacteria; Actinobacteridae; Actinomycetales; Corynebacterineae; Mycobacteriaceae; Mycobacterium.
REFERENCE 1 (residues 1 to 200)
AUTHORS Cole,S.T., Brosch,R., Parkhill,J., Garnier,T., Churcher,C., Harris,D., Gordon,S.V., Eiglmeier,K., Gas,S., Barry III,C.E., Tekaia,F., Badcock,K., Basham,D., Brown,D., Chillingworth,T., Connor,R., Davies,R., Devlin,K., Feltwell,T., Gentles,S., Hamlin,N., Holroyd,S., Hornsby,T., Jagels,K., Krogh,A., McLean,J., Moule,S., Murphy,L., Oliver,S., Osborne,J., Quail,M.A., Rajandream,M.A., Rogers,J., Rutter,S., Seeger,K., Skelton,S., Squares,S., Sqares,R., Sulston,J.E., Taylor,K., Whitehead,S. and Barrell,B.G.
TITLE Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence
JOURNAL Nature 393 (6685), 537-544 (1998)
MEDLINE 98295987
REMARK Erratum:[[published erratum appears in Nature 1998 Nov 12;396(6707):190]]
REFERENCE 2 (residues 1 to 200)
AUTHORS Parkhill,J.
TITLE Direct Submission
JOURNAL Submitted (11-JUN-1998) Submitted on behalf of the Mycobacterium tuberculosis sequencing and mapping teams, Sanger Centre, Wellcome Trust Genome Campus, Hinxton, Cambridge CB10 1SA Unite de Genetique Moleculaire Bacterienne, Institut Pasteur, 28 rue du Docteur Roux, 75724 Paris Cedex 15, France E-mail: parkhill@sanger.ac.uk
COMMENT Notes:
Details of M. tuberculosis sequencing at the Sanger Centre are available on the World Wide Web.
(URL, http://www.sanger.ac.uk/Projects/M_tuberculosis/) CDS have been renumbered from the original cosmid submissions but the old gene designations are in brackets after the new gene numbers.
Gene prediction was based on a Hidden Markov Model of TB genes implemented in TBparse (Krogh) supplemented with visual inspection of positional base preference in codons, especially where there is an increase in the observed/expected third position G + C.
CAUTION: In some cases we may not have predicted the correct initiation codon. Where possible we choose an initiation codon (atg, gtg, or ttg) which is preceded by an upstream ribosome binding site sequence (optimally 5-13bp before the initiation codon). If this cannot be identified we choose the most upstream initiation codon.

FEATURES Location/Qualifiers
source 1..200
/organism="Mycobacterium tuberculosis"
/strain="H37Rv"
/db_xref="taxon:1773"
/clone="Y6G11"
Protein 1..200
/product="hypothetical protein Rv3557c"
CDS 1..200
/gene="Rv3557c"

```
                     /note="Rv3557c, (MTCY06G11.04c), len: 200 aa. Probable
                     transcriptional repressor, similar eg to
                     Z95556|MTCY07A7_12 Mycobacterium tuberculosis (215 aa)
                     fasta scores,  opt: 215 z-score: 279.5 E(): 4.9e-08; 35.1%
                     identity in 148 aa overlap; and YIXD_BACSU P32398
                     hypothetical transcriptional regulatory protein (191 aa),
                     fasta scores, opt: 169, E(): 4.2e-05, (23.9% identity in
                     188 aa overlap)"
                     /db_xref="SPTREMBL:P96839"
                     /coded_by="complement(Z92774:2275..2877)"
                     /transl_table=11
ORIGIN
        1 mdrvagqvns rrgellelaa amfaerglra ttvrdiadga gilsgslyhh faskeemvde
       61 llrgfldwlf aryrdivdst anplerlqgl fmasfeaieh hhaqvviyqd eaqrlasqpr
      121 fsyiedrnkq qrkmwvdvln qgieegyfrp dldvdlvyrf irdttwvsvr wyrpggplta
      181 qqvgqqylai vlggitkegv
//
```

Save the above report in Macintosh Text format

NCBI Entrez **Protein QUERY** BLAST Entrez ?

Other Formats: FASTA | Graphic

Links: DNA | Related Sequences

```
LOCUS       2984362       192 aa                              03-SEP-1998
DEFINITION  transcriptional regulator (TetR/AcrR family).
ACCESSION   2984362
PID         g2984362
DBSOURCE    GENBANK: locus AE000776, accession AE000776
KEYWORDS    .
SOURCE      Aquifex aeolicus.
  ORGANISM  Aquifex aeolicus
            Eubacteria; Aquificales; Aquificaceae; Aquifex.
REFERENCE   1  (residues 1 to 192)
  AUTHORS   Deckert,G., Warren,P.V., Gaasterland,T., Young,W.G., Lenox,A.L.,
            Graham,D.E., Overbeek,R., Snead,M.A., Keller,M., Aujay,M.,
            Huber,R., Feldman,R.A., Short,J.M., Olson,G.J. and Swanson,R.V.
  TITLE     The complete genome of the hyperthermophilic bacterium Aquifex
            aeolicus
  JOURNAL   Nature 392, 353-358 (1998)
REFERENCE   2  (residues 1 to 192)
  AUTHORS   Deckert,G., Warren,P.V., Gaasterland,T., Young,W.G., Lenox,A.L.,
            Graham,D.E., Overbeek,R., Snead,M.A., Keller,M., Aujay,M.,
            Huber,R., Feldman,R.A., Short,J.M., Olson,G.J. and Swanson,R.V.
  TITLE     Direct Submission
  JOURNAL   Submitted (25-JUL-1997) Diversa Corporation, Genomics, San Diego,
            CA 92121
COMMENT     Method: conceptual translation.
FEATURES             Location/Qualifiers
     source          1..192
                     /organism="Aquifex aeolicus"
                     /strain="VF5"
                     /db_xref="taxon:63363"
     Protein         1..192
                     /product="transcriptional regulator (TetR/AcrR family)"
     CDS             1..192
                     /gene="acrR2"
                     /coded_by="AE000776:12906..13484"
                     /transl_table=11
ORIGIN
        1 myillfmgek rsdtkekils salklfskkg fkettikdia kevgitegai yrhftskeei
       61 iksllesitk elrhkleval qrgetdeeil esivdtlidy afsnpesfrf lnlyhllkey
      121 gevknlpgel ilkflnglyl krklktypei alavvtgsve rvfifkernf ldydeetikk
      181 elkkvlksai la
//
```

Save the above report in Macintosh | Text format

NCBI Entrez **Protein QUERY** BLAST Entrez ?

Other Formats: FASTA | Graphic

Links: MEDLINE | Related Sequences

```
LOCUS       730078         210 aa                              01-FEB-1995
DEFINITION  REGULATORY PROTEIN MTRR.
ACCESSION   730078
PID         g730078
DBSOURCE    SWISS-PROT: locus MTRR_NEIGO, accession P39897
            class: standard.
            created: Feb 1, 1995.
            sequence updated: Feb 1, 1995.
            annotation updated: Feb 1, 1995.
            xrefs: gi: 452332, gi: 438189, gi: 541020
            xrefs (non-sequence databases): PROSITE PS01081
KEYWORDS    TRANSCRIPTION REGULATION; DNA-BINDING; REPRESSOR.
SOURCE      Neisseria gonorrhoeae.
  ORGANISM  Neisseria gonorrhoeae
            Eubacteria; Proteobacteria; beta subdivision; Neisseriaceae;
            Neisseria.
REFERENCE   1  (residues 1 to 210)
  AUTHORS   Pan,W. and Spratt,B.G.
  TITLE     Regulation of the permeability of the gonococcal cell envelope by
            the mtr system
  JOURNAL   Mol. Microbiol. 11 (4), 769-775 (1994)
  MEDLINE   94254732
  REMARK    SEQUENCE FROM N.A.
            STRAIN=FA19
COMMENT     [FUNCTION] PUTATIVE REPRESSOR OF MTRC GENE. CONTROLS THE
            PERMEABILITY OF THE CELL ENVELOPE TO HYDROPHOBIC COMPOUNDS SUCH AS
            ANTIBIOTICS AND DETERGENTS.
            [SIMILARITY] BELONGS TO THE TETR/ACRR FAMILY OF TRANSCRIPTIONAL
            REGULATORS.
FEATURES             Location/Qualifiers
     source          1..210
                     /organism="Neisseria gonorrhoeae"
                     /db_xref="taxon:485"
                     1..210
     Protein         1..210
                     /product="REGULATORY PROTEIN MTRR"
     Site            32..51
                     /note="H-T-H MOTIF."
                     /site_type="dna-binding"
     Region          105
                     /note="H -> Y: IN PENICILLIN-RESISTANT ISOLATES."
                     /region_name="Variant"
ORIGIN
        1 mrktktealk tkehlmlaal etfyrkgiar tslneiaqaa gvtrgalywh fknkedlfda
       61 lfqricddie nciaqdaada eggswtvfrh tllhfferlq sndihykfhn ilflkcehte
      121 qnaaviaiar khqaiwreki tavlteaven qdladdldke tavifikstl dgliwrwfss
      181 gesfdlgkta priigimmdn lenhpclrrk
//
```

Save the above report in Macintosh | Text format

BMJ 1998;316:166 (17 January)

Editorials

Is measles infection associated with Crohn's disease?

The current evidence does not prove a causal link

- Send a response to this article
- Related letters in BMJ
- PubMed citation
- Related articles in PubMed
- Download to Citation Manager
- This article has been cited by other articles
- Search Medline for articles by:
  Metcalf, J.
- Alert me when:
  New articles cite this article

- Collections under which this article appears:
  Gastroenterology:
  Other Gastroenterology
  Infectious Diseases:
  Other Infectious Diseases

The cause of Crohn's disease is likely to be multifactorial, and great interest was generated by two Swedish studies suggesting a high risk of Crohn's disease in those exposed to measles in utero.[1] [2] The report in this week's issue from Nielsen et al (p 196),[3] however, is not alone in suggesting that there is no increased risk.

The two Swedish papers studied largely the same group of patients. Both studies were the result of two index cases of Crohn's disease noted to have been exposed to measles in utero (accounting for two out of four cases in the second study). The first report, in 1994, compared the expected and observed month of birth in patients with Crohn's disease born in 1945-54 in relation to the peak months of measles epidemics. The standardised incidence ratio was 1.46 (95% confidence interval 0.83 to 2.21) for future development of Crohn's disease for births during the three months after the peak incidence of measles. The second paper, in 1996, described a study of maternal measles infection in a cohort of 25 000 babies born in 1940-9.[2] Of four such cases three subsequently developed Crohn's disease.

In apparent support of the hypothesis, Thompson et al found a relative risk of 3.01 (1.45 to 6.23) for Crohn's disease among a British cohort of people vaccinated with live attenuated measles vaccine compared with a matched, unvaccinated group.[4] However, up to 74% of the original cohort were lost to follow up, and methods of follow up varied between the groups. This report led to concerns that vaccination with live, attenuated measles vaccine could confer the same risk as exposure to measles in utero.[5]

Now, however, four further studies have failed to confirm evidence of an association. Nielsen et al examined the health records of all possible cases of measles in pregnancy admitted to an infectious diseases hospital in the Copenhagen area in 1915-66.[3] The offspring of 25 women who had measles during pregnancy were identified, and none had developed Crohn's disease. In 1995 Hermon-Taylor et al compared the incidence of Crohn's disease with notifications of measles infection in England and Wales, including data after the introduction of measles vaccines.[6] They found no association. Also in 1997 Jones et al reported a case-control study of a large cohort of individuals exposed to viral infections during gestation, including 47 people exposed to measles in utero.[7] Follow up data on 88% found no cases of inflammatory bowel disease in the index cases, but two among the controls (one with Crohn's disease). A case-control study by Feeney et al in 1997 compared measles vaccination rates in 140 patients with inflammatory bowel disease (83 with Crohn's disease) and matched controls and found no association.[8]

To reconcile these discrepancies we need an understanding of the investigation of causation. Significant

associations were established in the original studies, but associations may be artefactual, indirect, or causal. Artefactual associations may result from chance. The inclusion of index cases which have generated the hypothesis leads to reporting bias, especially if the numbers are small. Spurious associations may also result from differences in methods and completeness of data collection and recall bias (cases more often recall exposure to possible causal factors than controls). Some of these factors may have affected Thompson's vaccination study.[4] An indirect association is one in which the factor and disease are associated through a common third factor, such as malaria and altitude, linked through mosquitoes. There are no apparent indirect links in these studies.

A refinement of Koch's postulates has led to the development of six criteria to evaluate the likelihood that an association is causal, the first three of which are the most important.[9] Firstly, the greater the strength of the association (the higher the relative risk) the more likely it is that a factor is causal. A dose-response gradient and a consistent association—that is, one repeated in other studies—also suggest causality. The specificity of the association—whether the occurrence of the factor predicts the presence of the disease—the correct temporal association, and the biological plausibility of the association are also relevant. Only the last two criteria are met by the Swedish studies.

Thus, several recent studies of the association between measles and Crohn's disease have failed to confirm the original association, suggesting that the original finding was artefactual. The theory of measles as a causative factor in the development of Crohn's disease therefore cannot be upheld and should remind us of the need for rigorous methodological review when causal associations are proposed.

Jane Metcalf, *Senior registrar in gastroenterology* [a]

[a] Gloucestershire Royal Hospital,Gloucester GL1 3NN

---

1. Ekbom A, Wakefield AJ, Zack M, Adami HO. Perinatal measles infection and subsequent Crohn's disease. *Lancet* 1994;344:508-10. [Medline]
2. Ekbom A, Daszak P, Kraaz W, Wakefield AJ. Crohn's disease after in-utero measles virus exposure. *Lancet* 1996;348:515-7. [Medline]
3. Nielsen LLW, Nielsen NM, Melbye M, Sodermann M, Jacobsen M, Aaby P. Exposure to measles in utero and Crohn's disease: a Danish register study. *BMJ* 1998;316:196-7. [Full Text]
4. Thompson NP, Montgomery SM, Pounder RE, Wakefield AJ. Is measles vaccination a risk factor for inflammatory bowel disease? *Lancet* 1995;345:1071-4. [Medline]
5. Calman KC. Measles vaccination as a risk factor for inflammatory bowel disease. *Lancet* 1995;345:1362-4.
6. Hermon-Taylor J, Ford S, Sumar N, Millar D, Doran T, Tizard M. Measles virus and Crohn's disease. *Lancet* 1995;345:922-3.
7. Jones P, Fine P, Piracha S. Crohn's disease and measles. *Lancet* 1997;349:473.
8. Feeney M, Clegg A, Winwood P, Snook J. A case control study of measles vaccination and inflammatory bowel disease. *Lancet* 1997;350:764-6. [Medline]
9. Mausner JS, Kramer S, eds. *Mausner and Bahn epidemiology. An introductory text.* Philadelphia: WB Saunders Company, 1985.

This article has been cited by other articles:

- Nicoll, A., Elliman, D., Ross, E. (1998). MMR vaccination and autism 1998. *BMJ* 316: 715-716 [Full text]

Related letters in BMJ:

Measles, measles vaccination, and Crohn's disease
Elizabeth Miller, Pauline Waight, R G Pebody, M Paunio, P Ruutu, Ross Lawrenson, and Richard Farmer
BMJ 1998 316: 1745. [Letter]

- Send a response to this article
- Related letters in BMJ
- PubMed citation
- Related articles in PubMed
- Download to Citation Manager
- Search Medline for articles by:
  Metcalf, J.
- Alert me when:
  New articles cite this article

- Collections under which this article appears:
  Gastroenterology:
  Other Gastroenterology
  Infectious Diseases:
  Other Infectious Diseases

NCBI Entrez **Protein QUERY** BLAST Entrez ?

Other Formats: FASTA | Graphic

Links: Related Sequences

```
LOCUS       481591         190 aa                                  20-FEB-1995
DEFINITION  hypothetical protein 4 - Clostridium pasteurianum.
ACCESSION   481591
PID         g481591
DBSOURCE    PIR: locus S38906
            summary: #length 190 #molecular-weight 21692 #checksum 8972.
            PIR dates: 20-Feb-1995 #sequence_revision 20-Feb-1995 #text_change
            20-Feb-1995.
KEYWORDS    .
SOURCE      Clostridium pasteurianum.
  ORGANISM  Clostridium pasteurianum
            Eubacteria; Firmicutes; Low G+C gram-positive bacteria;
            Clostridiaceae; Clostridium.
REFERENCE   1  (residues 1 to 190)
  AUTHORS   Meyer, J.
  TITLE     Direct Submission
  JOURNAL   Submitted (??-NOV-1993) to the EMBL Data Library
FEATURES             Location/Qualifiers
     source          1..190
                     /organism="Clostridium pasteurianum"
                     /db_xref="taxon:1501"
     Protein         1..190
                     /product="hypothetical protein 4"
ORIGIN
        1 mnktkdnify saikvfsnng yngatmdeia snagvakgtl yyhfkskeei fkyiieegvn
       61 lmkneideat dkektalekl kavcrvqlnl iyknrdffkv iasqlwgkel rqlelrdimr
      121 nyvvhieefv kdameagsik kgnslfvaya flgtlcsvsl yevinaendn inntienlmn
      181 yilngiglqn
//
```

Save the above report in Macintosh ▼ Text ▼ format